Serial No. 10/612,176 June 1, 2005 Page 2 of 20

## **Amendments**

Claim 1 (Previously Amended): A compound having the formula (I):

$$R^{1}$$
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{28}$ 
 $R^{7}$ 
 $R^{11}$ 
 $R^{11}$ 

or a pharmaceutically acceptable salt or solvate thereof, wherein

 $Ar^{1}$  and  $Ar^{2}$  are each independently selected from the group consisting of  $(R^{19})_{n7}$ -heteroaryl- and

 $\chi^1$  is selected from the group consisting of –O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>12</sup>-, -N(COR<sup>12</sup>)- and –N(SO<sub>2</sub>R<sup>15</sup>)-;

R<sup>1</sup>, R<sup>3</sup> and R<sup>5</sup> are each independently selected from the group consisting of H and C<sub>1</sub>-C<sub>5</sub> alkyl;

 $R^2$ ,  $R^4$  and  $R^6$  are each independently selected from the group consisting of H, -CONR<sup>13</sup>R<sup>14</sup> and -(CH<sub>2</sub>)<sub>n1</sub>-G; wherein G is selected from the group consisting of H, -CF<sub>3</sub>, -CHF<sub>2</sub>, -CH<sub>2</sub>F, -OH, -O-(C<sub>1</sub>-C<sub>6</sub>)alkyl, -SO<sub>2</sub>R<sup>13</sup>, -O-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -NR<sup>13</sup>R<sup>14</sup>, -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, -NR<sup>13</sup>SO<sub>2</sub>R<sup>15</sup>, -NR<sup>13</sup>COR<sup>12</sup>, -NR<sup>12</sup>(CONR<sup>13</sup>R<sup>14</sup>), -CONR<sup>13</sup>R<sup>14</sup>, -COOR<sup>12</sup> and C<sub>3</sub>-C<sub>8</sub> cycloalkyl; or

 $R^1$  and  $R^2$ , taken together with the carbon to which they are attached, form a  $C_3\text{-}C_6$  cycloalkyl ring; or

R1 and R2, taken together with the carbon to which they are attached, form a

group; or

R3 and R4, taken together with the carbon to which they are attached, form a

Serial No. 10/612,176 June 1, 2005 Page 3 of 20

> ₹<u></u>; ₹

group; or

R<sup>5</sup> and R<sup>6</sup>, taken together with the carbon to which they are attached, form a

<u>کے 3</u>

group;

 $R^7$  and  $R^{11}$  are each independently selected from the group consisting of H,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $(R^{16})_{n7}$ -aryl-,  $(R^{19})_{n7}$ -heteroaryl-, -COOR<sup>29</sup>, -CONR<sup>21</sup>R<sup>22</sup>, -CON( $R^{21}$ )(CH<sub>2</sub>)<sub>n</sub>- $G^1$ , -S(O)<sub>n5</sub>(CH<sub>2</sub>)<sub>n</sub>- $G^1$ , -S(O)<sub>n5</sub>R<sup>13</sup>, -CO(CH<sub>2</sub>)<sub>n</sub>- $G^1$  and -(CH<sub>2</sub>)<sub>n1</sub>- $G^1$ ; wherein

n is 0-4, and

 $G^{1} \text{ is selected from the group consisting of H, -OH, } (C_{1}\text{-}C_{6}) \text{alkyl}, \\ -O\text{-}(C_{1}\text{-}C_{6} \text{ alkyl}), -S(O)_{n5}R^{13}, -O\text{-}(C_{3}\text{-}C_{8} \text{ cycloalkyl}), -NR^{13}R^{14}, \\ -SO_{2}NR^{13}R^{14}, -NR^{13}SO_{2}R^{15}, -NR^{13}COR^{12}, -NR^{12}(CONR^{13}R^{14}), \\ -OC(=O)R^{12}, -CONR^{13}R^{14}, -COOR^{12}, C_{3}\text{-}C_{8} \text{ cycloalkyl, -CF}_{3}, \\ (R^{16})_{n7}\text{-aryl-O-, } (R^{16})_{n7}\text{-aryl-, } (R^{19})_{n7}\text{-heteroaryl-, } \\ (R^{19})_{n7}\text{-heterocycloalkyl- and alkenyl, and}$ 

provided that, when n is 0, then  $G^1$  is selected from the group consisting of H,  $(C_1\text{-}C_6)$ alkyl, alkenyl, -CONR<sup>13</sup>R<sup>14</sup>, -COOR<sup>12</sup>,  $C_3\text{-}C_8$  cycloalkyl, -CF<sub>3</sub>,  $(R^{16})_{n7}$ -aryl-,  $(R^{19})_{n7}$ -heteroaryl-, and  $(R^{19})_{n7}$ -heterocycloalkyl-; and

provided that, when  $n_1$  is 1, then  $G^1$  is selected from the group consisting of H,  $(C_1\text{-}C_6)$ alkyl, alkenyl,  $-S(O)_{n5}R^{13}$ ,  $-SO_2NR^{13}R^{14}$ ,  $-CONR^{13}R^{14}$ ,  $-COOR^{12}$ ,  $C_3\text{-}C_8$  cycloalkyl,  $-CF_3$ ,  $(R^{16})_{n7}$ -aryl-,  $(R^{19})_{n7}$ -heteroaryl- wherein said heteroaryl ring is bound by a ring carbon to the  $-(CH_2)_{n1}$ - group, and  $(R^{19})_{n7}$ -heterocycloalkyl- wherein said heterocycloalkyl ring is bound by a ring carbon to the  $-(CH_2)_{n1}$ -group; or

R<sup>7</sup> and R<sup>11</sup>, taken together with the nitrogen to which they are attached, form a 5-7 membered heterocycloalkyl ring of the following formula:

Serial No. 10/612,176 June 1, 2005 Page 4 of 20

R<sup>7</sup> and R<sup>11</sup>, taken together with the nitrogen to which they are attached, form a 5-membered ring having the formula (A) or (B):

$$\langle N \rangle$$
 or  $\langle N \rangle$   $\langle N \rangle$ 

X is selected from the group consisting of  $-NR^{20}$ -,  $-N(CONR^{13}R^{14})$ -,  $-N(CO_2R^{13})$ -,  $-N(SO_2R^{15})$ -,  $-N(COR^{12})$ -,  $-N(SO_2NHR^{13})$ -, -O-, -S-, -SO-,  $-SO_2$ -,  $-CF_2$ -,  $-CH_2$ -, and  $-C(R^{12})F$ -;

 $R^8$ ,  $R^9$  and  $R^{10}$  are each independently selected from the group consisting of H,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $-OR^{12}$ , halogen, -CN,  $-NO_2$ ,  $-CF_3$ ,  $-CHF_2$ ,  $-CH_2F$ ,  $-OCF_3$ ,  $-OCHF_2$ ,  $-OCH_2F$ ,  $-COOR^{12}$ ,  $-CONR^{21}R^{22}$ ,  $-NR^{21}COR^{12}$ ,  $-NR^{21}CO_2R^{15}$ ,  $-NR^{21}CONR^{21}R^{22}$ ,  $-NR^{21}SO_2R^{15}$ ,  $-NR^{21}R^{22}$ ,  $-SO_2NR^{21}R^{22}$ ,  $-S(O)_{n5}R^{15}$ ,  $(R^{16})_{n7}$ -aryland  $(R^{19})_{n7}$ -heteroaryl-;

R<sup>12</sup> is selected from the group consisting of H, C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

 $R^{13}$  and  $R^{14}$  are each independently selected from the group consisting of H<sub>1</sub>  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_3$  alkyl-O-CH<sub>3</sub>,  $C_3$ - $C_8$  cycloalkyl,  $(R^{19})_{n7}$ -aryl(CH<sub>2</sub>)<sub>n6</sub>- and  $(R^{19})_{n7}$ -heteroaryl-(CH<sub>2</sub>)<sub>n6</sub>-; or

R<sup>13</sup> and R<sup>14</sup>, taken together with the nitrogen to which they are attached, form a 4-7 membered ring containing from 0-3 additional heteroatoms selected from the group consisting of –O-, -S- and –NR<sup>12</sup>-;

 $R^{15}$  is C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl or -CF<sub>3</sub>;

R<sup>16</sup> is 1 to 3 substituents each independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halogen and -CF<sub>3</sub>;

 $R^{19}$  is 1 to 3 substituents each independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -OH, halogen, -CN, -NO<sub>2</sub>, -C(O)CF<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>2</sub>, -CH<sub>2</sub>F, -OCF<sub>3</sub>, -OCH<sub>2</sub>F, -O-(C<sub>1</sub>-C<sub>6</sub> alkyl), -O-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl),

Serial No. 10/612,176 June 1, 2005 Page 5 of 20

-COOR<sup>12</sup>, -CONR<sup>21</sup>R<sup>22</sup>, -NR<sup>21</sup>R<sup>22</sup>, -NR<sup>21</sup>COR<sup>12</sup>, -NR<sup>21</sup>CO<sub>2</sub>R<sup>12</sup>, -NR<sup>21</sup>CONR<sup>21</sup>R<sup>22</sup>, -NR<sup>21</sup>SO<sub>2</sub>R<sup>15</sup> and -S(O)<sub>05</sub>R<sup>15</sup>,

R<sup>20</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>n6</sub>-heterocycloalkyl,

 $(R^{19})_{n7}$ -aryl $(CH_2)_{n6}$ - or  $(R^{19})_{n7}$ -heteroaryl- $(CH_2)_{n6}$ -;

 $R^{21}$  and  $R^{22}$  are each independently selected from the group consisting of H,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_8$  cycloalkyl and benzyl; or

 $R^{21}$  and  $R^{22}$ , taken together with the nitrogen to which they are attached, form a 4-7 membered heteroaryl ring containing from 0-3 additional heteroatoms selected from the group consisting of -O-, -S- and  $-NR^{12}$ -;

R<sup>23</sup> and R<sup>24</sup> are each independently selected from the group consisting of H, C<sub>1</sub>-C<sub>6</sub> alkyl and –CONR<sup>13</sup>R<sup>14</sup>; or

R<sup>23</sup> and R<sup>24</sup>, taken together with the carbon atom to which they are attached, form a

group;

 $R^{25}$ ,  $R^{26}$ ,  $R^{27}$  and  $R^{28}$  are each independently selected from the group consisting of H and  $C_1$ - $C_6$  alkyl; or

R<sup>25</sup> and R<sup>26</sup>, taken together with the carbon atom to which they are attached, form a

group; or

R<sup>27</sup> and R<sup>28</sup>, taken together with the carbon atom to which they are attached, form a

group;

R<sup>29</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

n<sub>1</sub> is 1-4;

n<sub>4</sub> is 0-2;

n<sub>5</sub> is 0-2;

Serial No. 10/612,176 June 1, 2005 Page 6 of 20

n<sub>6</sub> is 0-3;

n<sub>7</sub> is 0-3; and

provided that, when  $n_4$  is 0, and  $R^{25}$  and  $R^{26}$  are each H, then X is not –O-, -NR<sup>20</sup>- or –S-.

Claim 2 (Original): The compound of Claim 1 wherein X1 is -O-.

Claim 3 (Original): The compound of Claim 1 wherein Ar<sup>1</sup> and Ar<sup>2</sup> are each independently

Claim 4 (Original): The compound of Claim 3 wherein R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are each independently selected from the group consisting of H, -CH<sub>3</sub>, halogen and -CF<sub>3</sub>.

Claim 5 (Original): The compound of Claim 1 wherein

X<sup>1</sup> is -O-; and

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently

wherein  $R^8$ ,  $R^9$  and  $R^{10}$  are each independently selected from the group consisting of H, -CH<sub>3</sub>, halogen and -CF<sub>3</sub>.

Claim 6 (Original): The compound of Claim 1 wherein

Ar<sup>2</sup> is

Serial No. 10/612,176 June 1, 2005 Page 7 of 20

wherein,

R<sup>8</sup> is selected from the group consisting of H and F, and R<sup>9</sup> and R<sup>10</sup> are each independently selected from the group consisting of H, - CH<sub>3</sub>, F, Cl and -CF<sub>3</sub>.

Claim 7 (Original): The compound of Claim 6 wherein  $X^1$  is -O-; and  $R^3$ ,  $R^4$ ,  $R^{27}$  and  $R^{28}$  are each H.

Claim 8 (Original): The compound of Claim 6 wherein R<sup>5</sup> and R<sup>6</sup> are H.

Claim 9 (Original): The compound of Claim 7 wherein R<sup>7</sup> and R<sup>11</sup>, taken together with the nitrogen to which they are attached, form a 5-7 membered ring having the following formula:

$$R^{5}$$
 $R^{6}$ 
 $R^{25}$ 
 $R^{26}$ 
 $R^{26}$ 

Claim 10 (Original): The compound of Claim 1 having the formula

wherein R<sup>7</sup>, R<sup>8</sup> and R<sup>11</sup> are selected from the group consisting of:

Serial No. 10/612,176 June 1, 2005 Page 8 of 20

R <sup>8</sup>	R <sup>7</sup>	R <sup>11</sup>
Н	Н	Н
Н	Н	7.4
Н	Н	
Н	H	F F F
н	Н	
Н	Ĥ	
Н	Н	
н	Н	
Н	Н	7. O
Н	Н	
н	Н	
Н	Н	S S

Serial No. 10/612,176 June 1, 2005 Page 9 of 20

H	н	
н	Н	OH OH
н	H	7. S.
Н	н	L'A NH
н	Н	F <sub>3</sub> C
Н	H	ZZ S N
Н	Н	
Н	Н	
Н	н	
H	Н	
Н	Н	

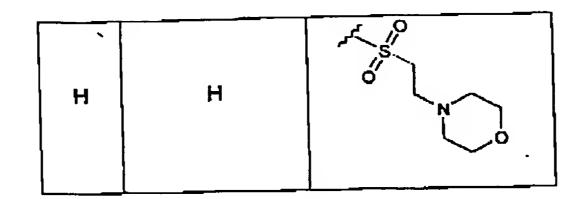
Serial No. 10/612,176 June 1, 2005 Page 10 of 20

Н	Н	Let N
н	:	
Н	. н	77 N N
Н	Н	7. T
Н	Н	NH <sub>2</sub>
н	ارگ	pri O-N
Н	S N	Prof.
F	Н	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
F	Н	H
F	Н	F F F
F	H	
F	H	

Serial No. 10/612,176 June 1, 2005 Page 11 of 20

	,	
F	Н	1 0 0 V
F	Н	
F	Н	3 O-N
F	Н	
Н	Н	J. C NH₂
Н	н	NH <sub>2</sub>
F	н	NH <sub>2</sub>
F	Н	NH <sub>2</sub>
Н	Н	NH <sub>2</sub>
Н	H	A SON
Н	. H	TH SH

Serial No. 10/612,176 June 1, 2005 Page 12 of 20



Claim 11 (Original): The compound of Claim 1 having the formula:

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>11</sup> are selected from the group consisting of:

R <sup>B</sup>	R <sup>1</sup>	R <sup>2</sup>	-NR <sup>7</sup> R <sup>11</sup>
Н	н	Н	N O
Н	Н	Н	N O
Н	н	Н	N O
Н	Н	Н	N NH
F	н	н	

Serial No. 10/612,176 June 1, 2005 Page 13 of 20

F	Н	н	N O
F	Н	Н	N O
Н	Н	Н	
Н	Н	ÇH₃	
Н	Н	СН₂ОН	
H	Н	н	H <sub>2</sub> N O
Н	Н	Н	H
Н	Н	Н	
н	Н	H	N O
Н	Н	Н	

Serial No. 10/612,176 June 1, 2005 Page 14 of 20

н	Н	Н	N N N N N N N N N N N N N N N N N N N
Н	Н	Н	N-NH

Claim 12 (Original): The compound of Claim 11 or the pharmaceutically acceptable salt or solvate thereof, wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>7</sup> R<sup>8</sup> and R<sup>11</sup> are selected from the group consisting of

R⁵	R <sup>1</sup>	R <sup>2</sup>	-NR <sup>7</sup> R <sup>11</sup>
Н	Н	Н	N O
Н	Н	Н	NH O
н	Н	CH₃	^j^ _N_O
Н	н	CH₂OH	N O
Н	Н	Н	N-NH.

Serial No. 10/612,176 June 1, 2005 Page 15 of 20

Claim 13 (Original): The compound of Claim 12 having the formula:

Claim 14 (Original): The compound of Claim 12 having the formula:

Claim 15 (Original): The compound of Claim 12 having the formula:

Claim 16 (Original): The compound of Claim 12 having the formula:

Serial No. 10/612,176 June 1, 2005 Page 16 of 20

Claim 17 (Original): The compound of Claim 12 having the formula:

Claim 18 (Previously Amended): A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of Claim 1, and a pharmaceutically acceptable carrier.

Claim 19 (Canceled).

Claim 20 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: respiratory diseases, inflammatory diseases, skin disorders, ophthalmalogical disorders, central nervous system conditions, addictions, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDs related dementia, Towne's disease, stress related disorders, obsessive/compulsive disorders, eating disorders, sleep disorders, mania, premenstrual syndrome, gastrointestinal

Serial No. 10/612,176 June 1, 2005 Page 17 of 20

disorders, atherosclerosis, fibrosing disorders, obesity, Type II diabetes, pain related disorders, bladder and genitourinary disorders, and nausea.

Claim 21 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive substance abuse, nociception, psychosis, schizophrenia, stress related disorder, obsessive/compulsive disorder, bulemia, anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and nausea.

Claim 22 (Withdrawn): A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, and an effective amount of at least one active ingredient selected from the group consisting of: other NK<sub>1</sub> receptor antagonists, selective serotonin reuptake inhibitors, dopamine receptor agonists, serotonin 5-HT<sub>2c</sub> receptor agonists, nociceptin receptor agonists, glucocorticoids and inhibitors of multidrug resistance protein 5, wherein said physiological disorder, symptom or disease is selected from the group consisting of: a respiratory disease, depression, anxiety, phobla, bipolar disorder, alcohol dependence, psychoactive substance abuse, nociception, psychosis, schizophrenia, stress related disorder, obsessive/compulsive disorder, bulemia, anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and nausea.

Claim 23 (Currently Amended): A method of treating emesis and/or nausea in a patient in need of such treatment comprising administering to said patient an 53850-1

Serial No. 10/612,176 June 1, 2005 Page 18 of 20

effective amount of at least one compound having the formula (I) of Claim 1 in combination with an effective amount of at least one serotonin 5-HT<sub>3</sub> receptor antagonist and/or at least one glucocorticoid.

Claim 24 (Withdrawn): The method of Claim 23 wherein said serotonin 5-HT<sub>3</sub> receptor antagonist is ondansetron and said glucocorticoid is dexamethasone.

Claim 25 (Withdrawn): The method of Claim 21, wherein the physiological disorder, symptom or disease is emesis, depression, anxiety or cough.

Claim 26 (Withdrawn): The method of Claim 25 wherein the physiological disorder, symptom or disease is depression or anxiety.

Claim 27 (Withdrawn): The method of Claim 26, further comprising administering to the patient an effective amount of at least one anti-depressant agent and/or at least one anti-anxiety agent.

Claim 28 (Withdrawn): The method of Claim 25 wherein depression is being treated and said method further comprises administering to the patient an effective amount of at least one selective serotonin reuptake inhibitor.

Claim 29 (Withdrawn): A method for antagonizing an effect of a Substance P at a neurokinin-1 receptor site or for blocking at least one neurokinin-1 receptor, in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1.

Claims 30-35 (Canceled).